Agricultural Biotechnology for Sustainable Productivity: A USAID Initiative for Plant Biotechnology in the Developing World

John Dodds
Department of Horticulture
Managing Director, Agricultural Biotechnology for Sustainable Productivity (ABSP)Project
Michigan State University, USA

Significant changes in world geography and politics and an ever-growing world population continue to put increasing pressure on food producers to deliver more food grown in the same or less space with greater nutritional value and less effect on the environment. At the same time, the understanding of plant biology and agriculture also has grown, providing the scientific community new tools with which to contribute to the resolution of these challenges.

One contribution of agricultural research is the development of new and improved germplasm and cultivars. The emergence of biotechnology and its integration with conventional plant breeding provides a new approach in addressing challenges to sustainable productivity not yet resolved by solely conventional means.

In the past decade, there has been a dramatic increase in the application of biotechnology in research programs supported through the international agricultural research system. Combining biotechnology and international crop improvement along with the means to integrate and apply new technologies will, in the long-term, provide new opportunities to bring the products of research to farmers and consumers around the world.

The capacity to take advantage of these new research opportunities has rapidly advanced among industrialized countries while developing countries are often unable to keep pace. The U.S. Agency for International Development (USAID) addresses the discrepancy in national science and technology capabilities through programs of collaboration among developed and developing countries which seek to enhance the sustainability of agricultural productivity.

HISTORICAL PERSPECTIVE

The first USAID centrally-funded initiative in this area was the Tissue Culture for Crops Project (TCCP) based at Colorado State University, Fort Collins, Colorado, USA, which sought to produce crops (wheat, rice and sorghum) tolerant to an array of stresses including salinity, drought and acid/aluminum

soil conditions. Some of the more significant accomplishments from TCCP were the registration and release of sorghum germplasm with improved tolerance to fall armyworm and to acid/aluminum soil conditions (other work on salt and drought tolerance is ongoing) and the construction of the International Plant Biotechnology Network (IPBNet).

In 1989, the USAID Office of Agriculture began a multistage review of opportunities to support biotechnology. External evaluation of TCCP was undertaken followed by the convening of an expert panel under the direction of the National Research Council (NRC). This panel produced a report, *Plant Biotechnology Research for Developing Countries,* published by the NRC in 1990, which looked at constraints on productivity in the developing world and relevant technologies to address those constraints in the near future.

The combined results of those investigations were then reviewed by USAID missions in developing countries and national and international agricultural programs. A new project in plant biotechnology was then designed which would bring together public sector and commercial research efforts in an integrated product-development program.

A NEW FOCUS, A NEW APPROACH: AGRICULTURAL BIOTECHNOLOGY FOR SUSTAINABLE PRODUCTIVITY INITIATIVE

The peer review process for proposals submitted to USAID through a formal "request for applications" resulted in the award of a cooperative agreement to Michigan State University, East Lansing, Michigan, USA, in September 1991, to implement the emergent new phase in USAID support for plant biotechnology. The purpose of the Agricultural Biotechnology for Sustainable Productivity (ABSP) project is "to mutually enhance U.S. and developing country institutional capacity for the use and management of biotechnology research in developing environmentally-compatible, improved germplasm through exchanges and training courses with developing country scientists."

MANAGEMENT APPROACH

Unlike basic research programs, ABSP takes an integrated approach to the development of specific research products and their transfer to developing country partners. In order to achieve integration, ABSP has set for itself the following management guidelines:

- Maintain a highly focused research program concentrating on specific crops and technologies.
- Implement a product-oriented research style which links public and private sector institutions in the U.S. and developing countries.
- Link product-oriented research to policy analysis of intellectual property and biosafety to ensure product commercialization in an environmentally and socially responsible manner.

•Maintain a geographical focus on specific centers of expertise; develop a critical mass for the multidisciplinary team which will transfer technology to national programs.

•Build a global network that provides access to information for developing and developed countries worldwide and serves as a forum for the exchange of ideas and information on biotechnology in relation to sustainable agriculture.

•Establish linkages with other organizations such as the Consultative Group for International Agricultural Research (CGIAR), U.S. Department of Agriculture Agricultural Research System (USDA/ARS) and the Biotechnology Industry Organization (BIO).

RESEARCH FOCUS

The goal of ABSP project research is to assist developing countries in adopting a wider application of biotechnology in order to address priority problems which represent specific constraints on agricultural productivity.

With a primary emphasis on working with developing country scientists to genetically engineer pest and pathogen resistance, ABSP focuses on the potential to reduce chemical input and produce high-quality plant material at a lower economic and environmental cost than conventional methods alone. The integration of new technologies, such as plant genetic transformation and bioreactor micropropagation, into the mainstream of international agriculture is envisioned. In achieving this goal, the economic and environmental sustainability of agricultural production systems will be improved and the quality of life enhanced by increasing the availability of food for consumption and marketing.

The research problems identified for inclusion in ABSP are those which conventional plant breeding alone cannot resolve. From the three regions of collaboration—Asia, Africa and Latin America—crops were chosen based on economic and nutritional significance coupled with severe pest or pathogen constraints on productivity. Targeted crops and constraints include: potato, constrained by potato tuber moth; sweet potato, constrained by sweet potato weevil; maize, constrained by the maize stem borer; cucurbits, constrained by zucchini yellow mosaic virus and other cucurbit potyviruses; and tomato, constrained by tomato yellow leaf curl virus and/or beet curly top virus.

ABSP has set research objectives which, when considered in their entirety, will reduce the constraints on productivity and broaden the application of biotechnology in developing countries:

• Transfer scientific knowledge and techniques to developing countries through postdoctoral fellowships.

• Assemble minigenes containing insect resistance genes *(Bacillus thuringiensis [Bt]* and proteinase inhibitor) driven by plant-specific regulatory elements.

• Genetically engineer potato, sweet potato and maize for resistance to insect pests in developing countries.

• Genetically engineer cucurbits with a virus coat protein gene for development of resistance to potyviruses.

• Genetically engineer tomato for resistance to viruses causing tomato yellow leaf curl disease.

• Demonstrate pest resistance of transgenic crops at the laboratory, greenhouse and field level, and integrate this into sustainable agricultural systems via collaborations with plant breeders, agronomists, statisticians, virologists and entomologists (with expertise in insect resistance management and integrated pest management).

• Transfer DNA Plant Technology Corporation's bioreactor micropropagation technology to private sector collaborators for the propagation of banana, pineapple, coffee and ornamental palm.

The U.S. Public Sector Research Team

ABSP is the first and only comprehensive biotechnology program to utilize collaborative research teams which encompass the public and private sectors, field agronomists, breeders, entomologists, virologists, molecular biologists, experts in biosafety and intellectual property protection, and other specialists committed to the equitable use of biotechnology in agricultural research globally. These teams provide the flexibility to implement partnerships in commercially-oriented research as easily as research at land-grant institutions, and through national and international agricultural research centers.

A consortium of three U.S. universities (Michigan State University, Cornell University, Texas A&M University) has developed a team of scientists with considerable expertise who will lead the research and training components set forth in the project objectives.

Mariam Sticklen, research director for the ABSP project, is a somatic cell geneticist and faculty member in the Departments of Crop and Soil Sciences and Entomology at Michigan State University (MSU). She has developed techniques in plant protoplast, cell and tissue culture (protoplast fusion by polyethylene glycol treatment, confirmation of the hybridity of fusion products by RFLP and enzyme analysis). Sticklen has transformed plant species using *Agrobacterium tumefaciens,* regenerated a significant number of fertile gramineous crops from *in vitro* cultures, and has transformed gramineous crops using the microprojectile bombardment system.

Developing country maize genotypes will be improved through plasmids constructed by Ray Wu, a biochemist, molecular geneticist and faculty member in the Section of Biochemistry, Molecular and Cell Biology at Cornell University, Ithaca, New York, USA. He has focused on isolating and characterizing cereal regulatory elements and using those elements to increase the expression of foreign genes in cereal crops.

Systems to transform plants from shoot apices have been developed by Roberta Smith, the Eugene Butler Professor in the Department of Soil and Crop Sciences at Texas A&M University, College Station, Texas, USA. She is a plant tissue culturist who has worked with the regeneration and development of salt-tolerant sorghum and the regeneration of several dicots. Potato, sweet potato and cucurbits will be engineered via the *Agrobacterium tumefaciensTi* plasmid method. Cereal crops are normally engineered via either biolistic tissue bombardment or the protoplast/polyethylene method of transformation; however, should a reproducible *Agrobacterium*-based transformation system be developed for maize, then the regulatory elements of a conserved gene will be used (such as rice actin, isolated by Ray Wu).

Transformation systems for cucurbit crops, which are of significant value to many developing country producers, have been developed by Rebecca Grumet, molecular virologist and faculty member in the Department of Horticulture at MSU, who has cloned viral coat proteins and transferred those genes into crop species.

Dave Douches, potato geneticist, breeder and faculty member in the Department of Crop and Soil Sciences at MSU, is carrying out research using *Bt* genes to transform potato germplasm, adapted to conditions in North Africa and the Middle East, for resistance to potato tuber moth. The MSU potato breeding program is positioned to integrate transformation technologies toward varietal development and commercialization.

ABSP/AGERI Collaboration

With the recent implementation of a cooperative agreement between ABSP and the Agricultural Genetic Engineering Research Institute (AGERI) in Cairo, Egypt, a number of collaborative research activities have resulted in the addition of Roger Beachy and Claude Fauquet, co-directors of the International Laboratory for Tropical Agricultural Biotechnology (ILTAB) at the Scripps Research Institute in La Jolla, California, USA to the research team. They will investigate the causal agent in tomato yellow leaf curl disease. Also, under the cooperative agreement with AGERI, Henry Munger, Rosario Prowidenti and Molly Kyle of Cornell University will team with Rebecca Grumet to develop transgenic cucurbits resistant to polyviruses. Ed Grafius, from the MSU Entomology Department will team with Dave Douches to develop transgenic potato germplasm resistant to potato tuber moth.

Public/Private Sector Relationships

Recently, many USAID foreign assistance programs have begun to effect a more active involvement on the part of private sector entities in the U.S. and its client countries. This involvement has particular benefit for programs in biotechnology since much of the technology is based in the private sector. USAID and its clients have a continuing interest in realizing the full scientific and institutional benefit of past investments in agricultural research. ABSP has the capability to assist in that realization in a number of ways.

Biotechnology is a cross-cutting science with orientation in both basic research and product development. ABSP is geared directly towards a transfer of technology leading to product development, with discretionary funds in the budget allocated as seed money for commercial product development of promising research results. The project fosters direct linkages between the public and private sectors including the U.S. university community (Michigan State University, Texas A&M University, Cornell University, University of Arizona) and other public sector institutions (Scripps Institute) as well as the private sector (DNA Plant Technology Corporation [DNAP], Cinnaminson, New Jersey, USA and ICI Seeds, Inc., Slater, Iowa, USA). Linkages with developing country institutions also include a variety of public institutions (KARI, Nairobi, Kenya; Central Research Institute for Food Crops [CRIFC], Bogor, Indonesia; University of Costa Rica; and AGERI, Cairo, Egypt) and the private sector (Agribiotecnologia de Costa Rica S.A., Alajuela, Costa Rica and Fitotek Unggul, Jakarta, Indonesia).

ABSP is attractive to developing countries which are seeking to move into the biotechnology arena but are unable to access technology which is quickly becoming more proprietary and "privatized." Private sector linkages have been established in ABSP from its initiation, so involvement with the project gives developing country programs direct access which can serve to drive reform within their own research system.

For example, DNAP has established two joint projects with private biotechnology companies under the ABSP project. The first joint project is with Agribiotecnologia de Costa Rica S.A., to explore advanced micropropagation methods (bioreactor cloning) for banana, pineapple, coffee and ornamental palms. The second involves a micropropagation company, Fitotek Unggul, and focuses on pineapple micropropagation.

The goal of these partnerships is to reduce the unit cost of the cloned plants by improving the micropropagation efficiency in each target species. If successful, these associations will create an opportunity for expansion of the micropropagation business and open doors toward vertical integration between producing and consuming markets.

A collaborative ABSP project between CRIFC and ICI Seeds, Inc. which through genetic engineering will develop insect-resistant tropical maize for Indonesia, is led in the U.S. by Martin Wilson, cell biologist and project leader at ICI Seeds, Inc. CRIFC is a public sector, developing country ABSP partner and ICI Seeds is a U.S. private sector partner.

The immediate goals of the three-year CRIFC/ICI collaboration are: 1. to produce commercially important insect resistant maize germplasm for Indonesia and 2. to train a team of Indonesian scientists in the genetic engineering enabling technology. In the longer term, it is hoped that commercialization of the germplasm can be achieved through partnership with a private company in Indonesia. ABSP represents an opportunity for ICI Seeds,

Inc. to address a target, in a developing country, in circumstances of shared cost and, as a consequence, lowered commercial risk. There is clearly synergy between the goals of USAID and ICI Seeds, Inc. in the development of a market for tropical maize in Indonesia. The outcome of a successful project could be an improvement in maize yields of up to 40 percent. The stability of yield would also be enhanced and, therefore, bring about a significant improvement in the reliability of the maize crop's contribution to the food supply in Indonesia.

NETWORKING

The research focus of ABSP is purposely narrow. Essentially, it addresses genetically engineered insect and virus resistance and the transfer of the bioreactor technology. There are three constraints on nine crops in four countries with 21 participating institutions. The management approach to networking is quite different. While services remain focused, an invitation to join the network is open to anyone who is interested.

The ABSP network publishes a quarterly newsletter, *BioLink;* provides access to literature; builds connections and promotes interaction among institutions and individuals through print and electronic media; organizes country-specific, regional and global workshops, conferences and symposia; coordinates internship programs in biosafety and intellectual property rights; and facilitates the building of linkages to other USAID projects such as the Bean/Cowpea Collaborative Research Support Program (CRSP) as well as the International Agriculture Research Centers (IARCs) and other institutions involved in international agricultural biotechnology research and development.

Promoting Human Resource Development

ABSP fosters an integrated approach to the promotion of biotechnology in developing countries by supporting human resource development and technology transfer through postdoctoral fellowships in research areas and through internships in technical and policy areas such as intellectual property and biosafety, which may have a direct impact on the success and adoption of the technology. By supporting consultants and developing country interns in biosafety and Intellectual Property Rights (IPR), ABSP hopes to establish a policy environment which encourages the growth and realization of the commercial potential of biotechnology. This support is important to developing country programs which recognize that increased capability in these areas is critical to the success of fledgling biotechnology programs.

Intellectual Property Rights

Licensing and intellectual property problems that arise in connection with the transfer to developing nations of technologies developed under the collaborative programs is addressed by John Barton, George E. Osborne Professor

of Law at Stanford Law School, Stanford, California, USA. He works with developing country officials and ABSP cooperators to assist in the drafting of international agreements between developed and developing country affiliates.

The ABSP management team works with developing country institutional leaders to identify candidates to participate as interns, under the direction of Barton, in intellectual property training programs. The program provides interns with access to expertise and information regarding IPR, not only from a legal perspective but also from the business perspective of private biotechnology companies. Interns receive hands-on training and develop case studies based upon current and expected situations in their home countries.

Biosafety

The USDA Animal and Plant Health Inspection Service (USDA/APHIS) Biotechnology, Biologies, and Environmental Protection (BBEP) division, Washington, DC, USA, is represented on the ABSP Technical Advisory Group by Sivramiah Shantharam. Scientific, technical and regulatory advice on matters related to biosafety, environmental safety, and the exportation and importation of genetically engineered organisms is provided by Shantharam through consultation on an institutional basis and through individual interaction as part of a biosafety internship program.

Biosafety interns from developing countries are trained at MSU and ICI Seeds, Inc. in the safe handling of transgenic materials in the laboratory, the greenhouse and the field. Interns design, plant and evaluate field test plots of transgenic crops and participate in a three-day workshop organized by Shantharam on the regulatory procedures and policy developed by USDA/APHIS-BBEP, the U.S. Environmental Protection Agency (EPA) and the U.S. Food and Drug Administration (FDA). Based upon their experiences, interns develop a draft set of biosafety regulations for their home country situation. The ABSP management team works with the developing country institutions to promote an active role for the interns in developing and implementing biosafety systems in their country and region.

Bio Link

The ABSP network office at MSU publishes a quarterly newsletter, *BioLink,* which disseminates information with regard to current activities and progress made in ABSP and other biotechnology research and development programs. It contains articles from the international centers, information services and agricultural biotechnology research programs from around the world. The original mailing list was derived from the IPBNet directory taking advantage of the efforts made by those who coordinated IPBNet and compiled the global database of active tissue culturists. The ABSP network has broadened its readership to include individuals and institutions involved in all phases of agricultural plant biotechnology. Currently, *BioLink* is distributed to 115 countries and over two thousand individuals and institutions; approximately half of

that distribution is to developing countries. The cost of producing the newsletter is covered by funding within the project so there is no subscription fee. New subscribers to *BioLink* from around the world are always welcome.

Trade Association Relationships

The ABSP commitment to building diverse linkages is exemplified in the project's role as sponsor of memberships in the Biotechnology Industry Organization (BIO), Washington, DC, USA. Developing country and U.S. institutions collaborating in ABSP, both public and private, were originally provided membership in the Association of Biotechnology Companies (ABC), a not-for-profit trade association, formed in 1983, with more than 350 members from 29 countries. ABC members include companies, universities and research institutions from throughout the world.

On July 1, 1993, ABC merged with the Industrial Biotechnology Association (IBA) to form the Biotechnology Industry Organization (BIO), the largest biotechnology trade association in the world. Institutions collaborating in ABSP, who had memberships in ABC, automatically became members of BIO. BIO facilitates interaction between member institutions through access to the organization's database and meetings, seminars and workshops. Current information on issues within the biotechnology industry is provided through informational videotapes, access to BioTechNet and BIO publications, and special attention by BIO's new Food and Agriculture Section. In addition, BIO will continue to organize an annual international exhibition and meeting similar to those sponsored in the past by ABC. At the 1993 ABC meeting, ABSP collaborators from focus countries held a session on the development and implementation of the project. At the 1994 BIO meeting, ABSP sponsored a concurrent session on building institutional linkages.

Industrial Seminar Series

Government, private sector and public institution leaders from ABSP focus countries have participated in a prototype Industrial Seminar Series. The purpose of the seminar series is to expose leaders in biotechnology research and development from developing countries with agricultural plant biotechnology programs of U.S. companies in order to interact with technical and business specialists responsible for the implementation and integration of those programs into the corporate structure. The prototype series met with enthusiastic reviews by participants, and a future series is being planned.

ACCESS TO ABSP THROUGH IN-COUNTRY USAID OFFICES

USAID is a complex and highly decentralized organization which gives support and assistance to developing countries in a number of ways. Central (core) funding through the regional and central bureaus, located in Washington, DC, USA, provide financial support to projects which are globally or regionally focused. ABSP is such a project and receives its funding from the

USAID Office of Agriculture, Bureau for Research and Development. Regional focus in ABSP, by virtue of the core award, is in Asia (Indonesia), Africa (Kenya) and Latin America (Costa Rica).

Individual USAID offices (missions), located in each country, retain a separate budget and portfolio of activities. Additionally, missions may access centrally funded projects, such as ABSP, through a process internally called a "buy-in," which involves a transfer of mission funds into a centrally located project's account. Buy-ins are designed to accomplish the specific initiatives mandated by the project in accord with the interests of the missions and their respective countries.

To date, ABSP has been enthusiastically received by various USAID missions and developing country national programs. A number of activities have been initiated whereby additional countries (e.g., Egypt), which were not designated for inclusion in ABSP under central funding (the core award), are being included through mission buy-ins, and countries which originally participated through central funding (e.g., Indonesia) have expanded their involvement through the buy-in process.

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